

SEQUENCE LISTING

<110> Walsh, Christopher
Chao, Hengjun
Burstein, Haim
Lynch, Carmel
Stepan, Tony
Munson, Keith

<120> Adeno-Associated Virus Vectors Encoding Factor VIII and
Methods of Using Same

<130> 35052/204375

<140> US 09/689,430

<141> 2000-10-12

<150> 60/158,780

<151> 1999-10-12

<160> 5

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 7944

<212> DNA

<213> Artificial Sequence

<220>

<223> Plasmid pDLZ6 encoding Homo sapiens BDD FVIII

<221> CDS

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<213> Homo sapiens B-domain deleted factor VIII

<220>

<223> Homo sapiens BDD FVIII

<400> 2

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
 1          5          10          15
Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20          25          30
Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
 35          40          45
Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
 50          55          60
Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile
 65          70          75          80
Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
 85          90          95
Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
100          105          110
His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
115          120          125
Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
130          135          140
Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
145          150          155          160
Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
165          170          175
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
180          185          190
Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
195          200          205
Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
210          215          220
Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
225          230          235          240

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Ala	Ala	Ser	Ala	Arg	Ala	Trp	Pro	Lys	Met	His	Thr	Val	Asn	Gly	Tyr	
				245					250					255		
Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Arg	Lys	Ser	Val	
			260					265					270			
Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Thr	Pro	Glu	Val	His	Ser	Ile	
		275					280					285				
Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	Asn	His	Arg	Gln	Ala	Ser	
	290					295					300					
Leu	Glu	Ile	Ser	Pro	Ile	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Leu	Leu	Met	
305					310					315					320	
Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	Gln	His	
				325					330					335		
Asp	Gly	Met	Glu	Ala	Tyr	Val	Lys	Val	Asp	Ser	Cys	Pro	Glu	Glu	Pro	
			340					345					350			
Gln	Leu	Arg	Met	Lys	Asn	Asn	Glu	Glu	Ala	Glu	Asp	Tyr	Asp	Asp	Asp	
		355					360					365				
Leu	Thr	Asp	Ser	Glu	Met	Asp	Val	Val	Arg	Phe	Asp	Asp	Asp	Asn	Ser	
	370					375					380					
Pro	Ser	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr	
385				390						395					400	
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro	
				405					410					415		
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn	
			420				425						430			
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met	
		435					440					445				
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu	
	450					455					460					
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu	
465				470					475						480	
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro	
				485					490					495		
His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys	
			500					505					510			
Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe	
		515					520					525				
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp	
	530					535					540					
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg	
545					550					555				560		
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu	
				565				570						575		
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val	
			580				585						590			
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu	
		595					600					605				
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp	
	610					615					620					
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val	
625					630					635					640	
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp	
				645				650						655		
Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe	
			660					665					670			
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	
			675				680						685			

Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser Thr Leu
 1140 1145 1150
 Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met Ala Ser
 1155 1160 1165
 Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln
 1170 1175 1180
 Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
 1185 1190 1195 1200
 Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala
 1205 1210 1215
 Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe
 1220 1225 1230
 Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly
 1235 1240 1245
 Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val
 1250 1255 1260
 Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn
 1265 1270 1275 1280
 Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser
 1285 1290 1295
 Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser
 1300 1305 1310
 Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln
 1315 1320 1325
 Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro
 1330 1335 1340
 Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro
 1345 1350 1355 1360
 Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr
 1365 1370 1375
 Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr
 1380 1385 1390
 Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His
 1395 1400 1405
 Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly
 1410 1415 1420
 Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu
 1425 1430 1435 1440
 Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile
 1445 1450 1455
 Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
 1460 1465 1470

<210> 3

<211> 7914

<212> DNA

<213> Artificial Sequence

<220>

<223> rAAV vector with canine B-domain deleted factor
VIII

<221> CDS

<222> (435)...(4730)

<400> 3

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gacgcccggg ctttgcccgg gcggcctcag tgagcgagcg agcgcgacaga gagggagtg 120
ccaactccat cactaggggt tcctcagatc tctttctaag taaacagtac atgaaccttt 180
accccgttgc tcggcaacgg cctgggtctgt gccaagtgtt tgctgacgca acccccactg 240
gctgggggctt ggccataggg catcagcgca tgcggatctc agtgtgggtt tgcaagagga 300
agcaaaaagc ctctccaccc aggcctggaa tgtttccacc caatgtcgag cagtgtgggt 360
ttgcaagagg aagcaaaaag cctctccacc caggcctgga ctcgacctcg agagtacttc 420
tagaaatacg agcc atg caa gta gag ctc tac acc tgc tgc ttt ctg tgc 470
          Met Gln Val Glu Leu Tyr Thr Cys Cys Phe Leu Cys
            1             5             10

```

```

ctt ttg ccc ttc agc ctt agt gcc acc aga aaa tac tac ctc ggt gca 518
Leu. Leu Pro Phe Ser Leu Ser Ala Thr Arg Lys Tyr Tyr Leu Gly Ala
      15             20             25

```

```

gtg gaa ctg tcc tgg gac tat atg caa agt gac ctg ctc agt gcg ctg 566
Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Leu Ser Ala Leu
      30             35             40

```

```

cac gcg gat aca agc ttt tct tcc agg gtg cca gga tct ttg cca ctc 614
His Ala Asp Thr Ser Phe Ser Ser Arg Val Pro Gly Ser Leu Pro Leu
      45             50             55             60

```

```

acc acg tca gtc acg tac aga aag act gtg ttt gta gag ttt aca gat 662
Thr Thr Ser Val Thr Tyr Arg Lys Thr Val Phe Val Glu Phe Thr Asp
      65             70             75

```

```

gac ctt ttc aac att gcc aag ccc agg cca ccg tgg atg ggc ctg ctg 710
Asp Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu
      80             85             90

```

```

ggg cct acc atc cag gct gag gtt tat gac aca gtg gtc att gtc ctt 758
Gly Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Val Leu
      95             100             105

```

```

aag aac atg gct tct cat cct gtc agc ctt cac gct gtt ggt gta tcc 806
Lys Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser
      110             115             120

```

```

tat tgg aaa gct tct gaa ggt gct gag tat gag gat cag acc agc caa 854
Tyr Trp Lys Ala Ser Glu Gly Ala Glu Tyr Glu Asp Gln Thr Ser Gln
      125             130             135             140

```

```

aag gag aag gaa gat gat aat gtc att cct ggt gaa agc cat acc tat 902
Lys Glu Lys Glu Asp Asp Asn Val Ile Pro Gly Glu Ser His Thr Tyr
      145             150             155

```

```

gtc tgg cag gtc ctg aaa gag aat ggc cca atg gcc tct gat cca cca 950
Val Trp Gln Val Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Pro
      160             165             170

```

```

tgt ctc acc tac tca tat ttt tca cac gtg gac ctg gtg aaa gac ctg 998
Cys Leu Thr Tyr Ser Tyr Phe Ser His Val Asp Leu Val Lys Asp Leu
      175             180             185

```

aat tca ggc ctc att gga gcc ctg ctg gtt tgc aaa gaa ggg agt ctg	1046
Asn Ser Gly Leu Ile Gly Ala Leu Leu Val Cys Lys Glu Gly Ser Leu	
190 195 200	
gcc aaa gaa agg aca cag acc ttg cag gaa ttt gtc cta ctt ttt gct	1094
Ala Lys Glu Arg Thr Gln Thr Leu Gln Glu Phe Val Leu Leu Phe Ala	
205 210 215 220	
gta ttt gat gaa ggg aaa agt tgg cac tca gaa aca aat gcg tct ttg	1142
Val Phe Asp Glu Gly Lys Ser Trp His Ser Glu Thr Asn Ala Ser Leu	
225 230 235	
aca cag gct gag gcc cag cat gag ctg cac acc atc aat ggc tat gta	1190
Thr Gln Ala Glu Ala Gln His Glu Leu His Thr Ile Asn Gly Tyr Val	
240 245 250	
aac agg tct ctg cca ggt ctt act gtg tgt cac aag aga tca gtc tat	1238
Asn Arg Ser Leu Pro Gly Leu Thr Val Cys His Lys Arg Ser Val Tyr	
255 260 265	
tgg cat gtg att gga atg ggc acc acc ccc gaa gtg cac tca att ttt	1286
Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe	
270 275 280	
ctc gaa ggt cac aca ttt ctt gtg agg aac cac cgc cag gcc tcc ttg	1334
Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu	
285 290 295 300	
gag atc tca cca att act ttc ctt act gct cag aca ttc ctg atg gac	1382
Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Phe Leu Met Asp	
305 310 315	
ctt ggc cag ttt cta ctg ttt tgt cat atc cct tcc cat caa cat gat	1430
Leu Gly Gln Phe Leu Leu Phe Cys His Ile Pro Ser His Gln His Asp	
320 325 330	
ggt atg gaa gct tat gtc aaa gta gat agc tgc cca gag gaa ccc cag	1478
Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln	
335 340 345	
ctg cgc atg aaa aat aat gaa gat aaa gat tat gat gat ggt ctt tat	1526
Leu Arg Met Lys Asn Asn Glu Asp Lys Asp Tyr Asp Asp Gly Leu Tyr	
350 355 360	
gat tct gac atg gac gta gtt agc ttt gat gac gac agc tct tct ccc	1574
Asp Ser Asp Met Asp Val Val Ser Phe Asp Asp Asp Ser Ser Ser Pro	
365 370 375 380	
ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act tgg gtc	1622
Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val	
385 390 395	
cac tat att gct gct gag gag gag gac tgg gac tat gct ccc tca ggc	1670
His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro Ser Gly	
400 405 410	

ccc acc ccc aat gat aga agt cat aaa aat ctg tat ttg aac aat ggt	1718
Pro Thr Pro Asn Asp Arg Ser His Lys Asn Leu Tyr Leu Asn Asn Gly	
415 420 425	
cct cag cgg att ggt aag aag tac aaa aaa gtc cga ttt gtg gca tac	1766
Pro Gln Arg Ile Gly Lys Lys Tyr Lys Lys Val Arg Phe Val Ala Tyr	
430 435 440	
aca gat gag aca ttt aag act cgt gaa gct att cag tat gaa tca gga	1814
Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln Tyr Glu Ser Gly	
445 450 455 460	
atc ctg gga cct tta ctt tat gga gaa gtt gga gac aca ctg ctg att	1862
Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile	
465 470 475	
ata ttt aag aat caa gcc agc cgg cca tat aac atc tac cct cat ggg	1910
Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly	
480 485 490	
atc aat tat gtc act cct ctg cac aca ggg aga ttg cca aaa ggt gtg	1958
Ile Asn Tyr Val Thr Pro Leu His Thr Gly Arg Leu Pro Lys Gly Val	
495 500 505	
aaa cat ttg aaa gat atg cca att ctg ccg gga gag ata ttc aag tat	2006
Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr	
510 515 520	
aaa tgg aca gtg acc gta gaa gat gga cca act aaa tca gat cct cgg	2054
Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp Pro Arg	
525 530 535 540	
tgc ctg acc cga tat tac tca agc ttc att aat ctg gag aga gat cta	2102
Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Ile Asn Leu Glu Arg Asp Leu	
545 550 555	
gct tca gga ctc att ggc cct ctt ctc atc tgc tac aaa gaa tct gta	2150
Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu Ser Val	
560 565 570	
gat caa aga gga aac cag atg atg tca gac aag aga aat gtc atc ctg	2198
Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val Ile Leu	
575 580 585	
ttt tct gta ttt gat gag aat cga agc tgg tac ctc aca gag aat atg	2246
Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu Asn Met	
590 595 600	
cag cgc ttc ctc ccc aat gca gat gta gtg cag ccc cat gac cca gag	2294
Gln Arg Phe Leu Pro Asn Ala Asp Val Val Gln Pro His Asp Pro Glu	
605 610 615 620	
ttc caa ctc tct aac atc atg cac agc atc aat ggc tat gtt ttt gac	2342
Phe Gln Leu Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val Phe Asp	
625 630 635	

aac ttg cag ctg tca gtt tgt ttg cat gag gtg gcg tac tgg tac att	2390
Asn Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp Tyr Ile	
640 645 650	
cta agt gtt gga gca caa act gac ttc ctg tct gtc ttc ttc tct gga	2438
Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe Ser Gly	
655 660 665	
tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctt acc ctc ttc	2486
Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr Leu Phe	
670 675 680	
cca ttc tca gga gaa act gtc ttc atg tca atg gaa aac cca ggt ctg	2534
Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro Gly Leu	
685 690 695 700	
tgg gtt ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc atg aca	2582
Trp Val Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly Met Thr	
705 710 715	
gcc tta ctg aag gtt tct agt tgt aac agg aac att gat gat tat tat	2630
Ala Leu Leu Lys Val Ser Ser Cys Asn Arg Asn Ile Asp Asp Tyr Tyr	
720 725 730	
gag gac aca tac gaa gat att cca act ccc ctg cta aat gaa aac aat	2678
Glu Asp Thr Tyr Glu Asp Ile Pro Thr Pro Leu Leu Asn Glu Asn Asn	
735 740 745	
gta att aaa cct aga agc ttc tcc cag aat tca agg cac cct agc act	2726
Val Ile Lys Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro Ser Thr	
750 755 760	
aag gaa aag caa ttg aaa atg aag aga gaa gat ttt gac atc tac ggc	2774
Lys Glu Lys Gln Leu Lys Met Lys Arg Glu Asp Phe Asp Ile Tyr Gly	
765 770 775 780	
gac tat gaa aat cag ggc ctc cgc agc ttt caa aag aaa aca cga cac	2822
Asp Tyr Glu Asn Gln Gly Leu Arg Ser Phe Gln Lys Lys Thr Arg His	
785 790 795	
tat ttc att gct gca gtg gag cgt ctc tgg gat tat ggg atg agt aga	2870
Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser Arg	
800 805 810	
tct ccc cat ata cta aga aac agg gct caa agt ggg gat gtc cag cag	2918
Ser Pro His Ile Leu Arg Asn Arg Ala Gln Ser Gly Asp Val Gln Gln	
815 820 825	
ttc aag aag gtg gtt ttc cag gaa ttt act gat gga tcc ttt act cag	2966
Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly Ser Phe Thr Gln	
830 835 840	
ccc tta tac cgt gga gaa ctg aat gaa cac ttg gga ctc ttg ggg cca	3014
Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly Leu Leu Gly Pro	
845 850 855 860	

tat ata aga gca gaa gtt gaa gac aat atc gtg gta act ttc aaa aac	3062
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Val Val Thr Phe Lys Asn	
865 870 875	
cag gcc tct cgt ccc tac tcc ttc tat tct agt ctt att tct tat gac	3110
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Asp	
880 885 890	
gaa gat gag gga caa gga gca gaa cct aga aga aag ttt gtc aac cct	3158
Glu Asp Glu Gly Gln Gly Ala Glu Pro Arg Arg Lys Phe Val Asn Pro	
895 900 905	
aat gaa acc aaa att tac ttt tgg aaa gtg cag cat cat atg gca ccc	3206
Asn Glu Thr Lys Ile Tyr Phe Trp Lys Val Gln His His Met Ala Pro	
910 915 920	
act aaa gat gag ttt gac tgc aaa gcc tgg gct tat ttt tct gat gtt	3254
Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val	
925 930 935 940	
gat ttg gag aaa gat gtg cac tca ggc ttg att gga ccc ctt ctg atc	3302
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile	
945 950 955	
tgc cgc agt aac aca ctg aac cct gct cat ggg aga caa gtg aca gtg	3350
Cys Arg Ser Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr Val	
960 965 970	
cag gag ttt gcc ctg gtt ttc act ata ttc gat gag act aag agc tgg	3398
Gln Glu Phe Ala Leu Val Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp	
975 980 985	
tac ttc act gaa aac ctg gaa agg aac tgt aga gct ccc tgc aat gtc	3446
Tyr Phe Thr Glu Asn Leu Glu Arg Asn Cys Arg Ala Pro Cys Asn Val	
990 995 1000	
cag aag gag gac cct act cta aaa gaa aac ttc cgc ttc cat gca atc	3494
Gln Lys Glu Asp Pro Thr Leu Lys Glu Asn Phe Arg Phe His Ala Ile	
1005 1010 1015 1020	
aac ggc tat gtg aag gat aca ctc cct ggc tta gta atg gct cag gat	3542
Asn Gly Tyr Val Lys Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asp	
1025 1030 1035	
caa aag gtt cga tgg tat ctg ctc agc atg ggc agc aac gaa aac att	3590
Gln Lys Val Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile	
1040 1045 1050	
cat tcc att cac ttc agt gga cat gtg ttc act gta cgg aaa aaa gag	3638
His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys Glu	
1055 1060 1065	
gaa tat aaa atg gca gtc tac aac ctc tat cca ggt gtt ttt gag act	3686
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr	
1070 1075 1080	

gtg gaa atg cta cca tcc caa gtt gga atc tgg cgg ata gaa tgc ctt	3734
Val Glu Met Leu Pro Ser Gln Val Gly Ile Trp Arg Ile Glu Cys Leu	
1085 1090 1095 1100	
atc ggc gag cac ctg caa gcc ggg atg agc act ctg ttt ctg gtg tac	3782
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Leu Phe Leu Val Tyr	
1105 1110 1115	
agc aag aag tgt cag act cca ctg ggg atg gct tcc gga cac att aga	3830
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg	
1120 1125 1130	
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag	3878
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys	
1135 1140 1145	
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag	3926
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys	
1150 1155 1160	
gat ccc ttt tcc tgg atc aag gtg gat ctc ttg gca ccg atg att att	3974
Asp Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile	
1165 1170 1175 1180	
cac ggc atc atg acc cag ggg gcc cgc cag aag ttc tcc agc ctc tac	4022
His Gly Ile Met Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr	
1185 1190 1195	
gtg tct cag ttt atc atc atg tac agt ctg gat ggc aac aag tgg cac	4070
Val Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Asn Lys Trp His	
1200 1205 1210	
agt tac cga ggg aat tcc acg ggg acc tta atg gtc ttc ttt ggc aac	4118
Ser Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn	
1215 1220 1225	
gtg gat tca tct ggg atc aaa cac aat att ttt aac cct ccg att att	4166
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile	
1230 1235 1240	
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Ser Tyr Leu Ser Ser Met Leu Ala Thr Trp Ser Pro Ser Gln Ala Arg	
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 Ser Thr Pro Val Arg Asn Arg Leu Glu Pro Pro Leu Val Ala Arg Tyr
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 50          55          60
Thr Tyr Arg Lys Thr Val Phe Val Glu Phe Thr Asp Asp Leu Phe Asn
 65          70          75          80
Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85          90          95
Gln Ala Glu Val Tyr Asp Thr Val Val Ile Val Leu Lys Asn Met Ala
 100         105         110
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala
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Asp Asp Asn Val Ile Pro Gly Glu Ser His Thr Tyr Val Trp Gln Val
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His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	Leu	Phe	Pro	Phe	Ser	Gly	675	680	685
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